PARTNERS HUMAN RESEARCH COMMITTEE
PROTOCOL SUMMARY

Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR

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PROTOCOL TITLE

Efficacy of the Quell Wearable Device for Chronic Low Back Pain

FUNDING

NeuroMetrix

VERSION DATE

10/25/2016

SPECIFIC AIMS

Concisely state the objectives of the study and the hypothesis being tested.

This proposed study is designed for patients with chronic low back pain. The overall aim of the study is to determine the effect of Quell wearable device to manage low back pain compared with no Quell wearable device. The Quell is battery powered with rechargeable batteries and is strapped to your upper calf with a velcro band. It has been cleared by the FDA for safety. It is designed to improve back pain by the principles of massage and vibration much like a traditional transcutaneous electrical nerve stimulator (TENS) unit. We will employ objective quantitative sensory testing (QST) measures of touch and pressure to assess pain sensitivity and to track each of the subjects using a smartphone pain app. A secondary goal is to help understand individual differences in response to using the Quell and identify specific demographic factors of age, pain duration, and physical function that may contribute to benefiting from the device among individuals diagnosed with chronic low back pain.

Research Objectives:

This is a low-risk trial designed to gather information about the use of the Quell to manage chronic low back pain. The primary outcome measures will be tolerability and changes in outcome.
1) Tolerability will be reflected in the portion of people that, when first testing the Quell, are not bothered by the use of the Quell, and feel they would be willing to use this device on a daily basis. Special attention will be given to reasons for dropout and noncompliance across different groups. Patients who discontinue use of the Quell will be encouraged to provide a reason, and attention will be given to understanding ease-of-use, personalized feedback, and perceived effect of the Quell.
2) Changes in outcome such as pain intensity, anxiety, sleep, and activity interference will be assessed. We will determine whether use of the Quell resulted in an increase in adverse outcomes. Although unanticipated, if safety issues are identified, changes will be made to the

protocol. Participants will have multiple opportunities to speak to study staff and to share any problems they encounter.

Study Hypotheses

1. We hypothesize that the Quell will be accepted and well tolerated by most patients and, given the opportunity, most patients will be willing to participate in using the Quell.
2. We hypothesize that the Quell will help in reducing pain, emotional distress, and activity interference caused by pain.

BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

Lower back pain is a common disorder that can be complex and multi-factorial, with contributions involving nerves, muscles and bones of the back. Pain can vary from a dull constant ache to a sudden sharp feeling. Low back pain that lasts longer than 3 months can be classified as chronic. The condition may be further classified by the underlying cause of the pain as mechanical, non-mechanical, or referred pain. There may also be involvement of central and peripheral nervous system pathoplasticity. In most episodes of lower back pain, the pain is due to mechanical problems such as muscle or joint strain. The incidence of low back pain is estimated to be as high as 9 to 12% of the general population at any given point in time, and nearly 25% report having had it at some point over any one-month period. About 40% of people have low back pain in their lives, with estimates as high as 80% among people in the developed world. Physical causes may include osteoarthritis, degeneration of the discs, or spinal disc herniation. Musculoskeletal mechanical low back pain may be due to muscle strain, muscle spasm, herniated nucleus pulposus, or spinal stenosis. Diffuse pain that does not change in response to particular movements, and is localized to the lower back without radiating beyond the buttocks, is classified as nonspecific, which is the most common classification. There are few accepted treatments for low back pain that do not involve prescription medication, manipulation, invasive procedures, or surgery. Similar to other chronic pain conditions, there is broad inter-patient variability in low back pain.

NeuroMetrix, Inc is a company that has developed a medical device designed to reduce painful symptoms and enhance movement without prescription medication, invasive procedures, or surgery. In particular, the Quell was developed for persons with chronic pain and joint discomfort. The device, with NeuroMetrix® technology, utilizes mild stimulation for 60 minute periods that serves to help individuals with persistent pain. This device is purported to activate the endogenous opioid system in the body, and to significantly reduce pain with daily use. This product is FDA cleared, with built in accelerometer measures, a rechargeable battery, and can deliver safe, effective pain relief. This proposed study will examine the benefit of this device among individuals with low back pain.

We have developed and implemented a smartphone pain app for iPhone and Android devices that includes medical and pain assessment items, daily assessment tracking, and 2-way messaging for persons with chronic pain. This program provides technology designed to better enable chronic pain patients and their providers to monitor level of pain, sleep, mood, and activity interference. The smartphone pain app was developed as an assessment and communication program in order to provide the best possible care for patients who suffer from chronic pain. The smartphone pain app would be used to monitor the subjects over the 3-month trial.

In psychophysical studies, individuals reporting persistent low back pain are characterized by enhanced pain sensitivity on quantitative sensory testing (QST), which refers to a set of psychophysical methods used to quantify somatosensory function. QST has been used for decades in a variety of research settings, often for the purpose of diagnosing and monitoring sensory neuropathies and pain disorders, as well as for the investigation of pain mechanisms, the characterization of somatosensory profiles in various pain disorders, and the elucidation of individual differences in pain sensitivity and pain modulation.

This proposed study is designed for patients with primary mechanical low back pain. The overall aim of the study is to determine the effect of the NeuroMetrix Quell to manage musculoskeletal chronic back pain compared with treatment as usual. We will employ objective QST measures to assess pain intensity and track each of the subjects using a smartphone pain app. A secondary goal is to help understand individual differences in response to using the Quell device and identify specific demographic factors of age, pain duration, and physical function that may contribute the most to benefit of this intervention for painful symptoms among individuals diagnosed with musculoskeletal low back pain. This is a preliminary study designed to investigate the feasibility of the Quell in benefiting persons with chronic back pain. If the results of this investigation reveal promising findings, then a longer trial with more subject numbers will be considered by the company. Because this is a feasibility study, no power analyses were conducted. Similar to other trials of this nature, we believe that the sample size of 30 subjects in each group followed for 3 months will allow for adequate preliminary comparison of outcome to determine whether a larger study is needed.

RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

We will recruit 69 patients with chronic low back pain and randomize each of the subjects to one of two treatment conditions: 1) Quell wearable device or 2) no Quell wearable device. All participants will be adults age 21 or older and diagnosed with chronic low back pain. Patients will be invited to participate if they own a smartphone phone (iPhone or Android device) and are able to download the pain app program onto their device. Patients will also be included if they (1) have chronic pain for > 3 months' duration, (2) average 4 or greater on a pain intensity scale of 0 to 10, and (3) are able to speak and understand English. Subjects who are planning medical interventions such as surgery or treatment with injections such as nerve blocks or steroid treatment are excluded from study participation. Patients will be equally randomized to treatment group (N=30) and control group (N=30) with treatment as usual using the pain app alone (control). All subjects will complete assessment measures and be followed for 3 months. Recruitment will not be restricted based on race or ethnicity. Efforts will be made to recruit at least 15% minorities. All participants will get assistance in downloading the pain app and have access to a research assistant (RA) who could answer any questions and help manage any problems that the individual may encounter. All participants will also be given QST testing at baseline. The QST test will consist of use of a pressure algometer for pressure pain threshold assessment using mechanical force to the trapezious muscles of both shoulders and forearms of both arms. We will also use punctate mechanical probes delivered to the middle finger of the right hand to assess pain windup. These measures have been standardized and

have been included in our previous studies. We will also use an enriched design by first having the potential subjects try on the Quell. If they feel that they would like to use the Quell they will be included in the study. If they dislike using the Quell on an initial exposure of 2 to 3 minutes then information will be collected of their age, ethnicity, and pain duration and the participants will be thanked for their interest in the study and dismissed.

Patients assigned to the experimental group (Quell wearable device) will be encouraged to use the Quell at least 120 minutes every day and to enter daily reports of how long they used the Quell through the pain app. All data will be stored on a secure server (Veracode tested) at BWH and messages will be sent via the 2-way messaging pain app program to help track use of the Quell. Patients who wish to discontinue the study will be allowed to do so at their request. If the participant is willing, we will meet with him or her to understand reasons for discontinuing the study and problem-solve to see if there is a way to keep following the individual. All subjects will be asked to complete mid-point assessments approximately 6 weeks after the start of the study. All subjects will also be asked to complete post-intervention assessments after 3 months. Each will be compensated $25 at baseline and $50 at study completion. Subjects in the Experimental group will be able to keep their Quell wearable device at the end of the study, and subjects in the Control group will be offered a Quell wearable device at the end of the study, if they are interested. It is expected that 15% of the subjects will dropout before completing the study and recruitment of 69 subjects will be needed.

Patient Measures: We will be tracking the patients using validated measures of pain (The Brief Pain Inventory - BPI), coping (Pain Catastrophizing Scale - PCS), level of disability (Pain Disability Index - PDI), mood (Hospital Anxiety and Depression Scale - HADS), healthcare utilization (monthly clinic and ED visits), and overall satisfaction (Satisfaction and qualitative questions).

Research Objectives: This is a 1-year trial designed to gather information about the use of the Quell wearable device for persons with chronic low back pain. We hypothesize that those assigned to using the Quell will report reduced pain compared with those in the control condition; with those using the Quell showing greatest benefit. We hypothesize that frequency of using the Quell (increased tolerability and adherence) will be correlated with greater reduction in pain. We hypothesize that the Quell will be safe to use and will demonstrate a reduction in healthcare utilization (reduced clinic and ED visits). Finally, based on preliminary analyses limited by few subject numbers, we will investigate whether certain individuals report greater benefit from using the Quell than others and, in particular, would predict that older adults with more intense and longer duration of pain will demonstrate most benefit.

Statistical Analysis Plan: Power calculations were performed to determine the probability of detecting clinically significant differences between treatment groups in the primary area of measurement: pain intensity. These calculations assumed a two-tailed test and alpha level of 0.025 confirming the hypotheses that the Quell would be associated with general overall improvement (e.g., more pain relief). A more rigorous $p<0.025$ significance level was established rather than $p<0.05$ because of the multiple observations. The power analyses revealed that a sample size of 60 subjects (30 per treatment group), gives the study a >80% probability of detecting a 1.5-point group difference on a 0-10 rating scale. Depending on the nature of the variables, chi-square, t-tests, and logistic regression analyses were conducted using Bonferroni correctional analyses. Group differences were assessed using repeated measures ANOVA and preliminary mixed linear regression model analyses, as appropriate.

Briefly describe study procedures. Include any local site restrictions, for example, "Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

It is expected that the study will be completed in approximately 1 year.

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

All participants will follow treatment of their low back pain according to standard of care and as recommended by the treating physician. The use of the Quell wearable device will represent an additional treatment. Those in the control condition will continue to be treated according to standard of care. All participants will be asked to use the smartphone pain app to monitor their progress.

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

Although the risks are perceived to be minimal, the following procedures have been put in place in order to comprehensively protect human subjects. Throughout the study, the Principal Investigator will be alerted to any complaints or adverse reactions that arise and will take appropriate steps to alleviate the difficulties as soon as possible. If an adverse event is reported to the Principal Investigator, he will work directly with the participant to ensure the matter is resolved to the satisfaction of the participant. Participants will be assured that they may discontinue the study at any time without penalty or prejudice. Any serious adverse events (i.e., those requiring intervention) among participants during the course of data collection will be reviewed by the Principal Investigator; if the adverse event is considered to be study-related, the details will be reported to the IRB.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

All contact with participants will be supervised by Dr. Jamison (PI). Precautions will be taken when contacting and communicating with subjects to ensure that their participation is kept confidential. All data will be password-protected or remain under lock and key. No names or other personal identifiers will be associated with particular responses or will be included in any reports that may arise from this research. The study manager will be trained to permit participants ample time to complete any forms/interviews and to avoid pressuring participants to provide particular responses. Patients will be assured that their decision to participate will not affect their medical treatment. An IRB will be convened to address issues of subject protection and to review consent forms. Throughout the study, investigators will be alert to any complaints

or adverse reactions and will take appropriate steps to alleviate the difficulties as soon as possible. Patients will be given the names and phone numbers of individuals to contact in the event of an emergency or a complaint or question regarding the conduct of the study.

Subjects will be closely monitored over the duration of the study for evidence of clinically significant distress or depression. Subjects will be closely followed by a study psychologist (PI) and subjects will instructed to maintain contact through the smartphone pain app, which will monitor daily levels of mood. We will assess for risk of depression at each time point of the study (phone call and clinic visit). The study staff is appropriately trained to take any necessary actions. The study will follow standard of care and therefore will not expose subjects to any risks outside of the standard effect of treatment. In the event of severe levels of depression, the Partners IRB will be notified and the subject will be withdrawn from the study as needed and monitored afterwards to ensure subject safety.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

The Quell wearable device is perceived to be of minimal risk for any adverse reaction, but all reactions will be carefully monitored and participants will be informed to discontinue use of the Quell if they experience any unwanted symptoms. There is also the risk to potential breach of confidentiality. All patient data collected through the study will be de-identified. There will be some burden of completing questionnaires and the need to complete daily diaries on the smartphone.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects." Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

For those in the Experimental condition, patients may find the Quell to be beneficial in reducing their pain.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

It is anticipated that the study risks will be viewed by participants as reasonable in relation to the likely benefits. There is no reason to suspect that provision of the Quell devices will be harmful

to the participants. In addition, participants will receive modest remuneration given the requirements of the study.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

Non-English speaking patients will be excluded from the study because the smartphone app and the validated questionnaires are currently only available in English.

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.pdf

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

Patients will initially be identified by their treating physician and giving information about the nature of the study. Flyers and handouts about the study will be available in the clinics. The study manager will consent the patients after all questions are answered.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

Study patients will receive a $25 check after baseline and a $50 check after post-treatment assessments for a total of $75. All participants will be offered a Quell to keep. Subjects in the control condition will be offered a Quell after completing the 3-month study monitoring period.

For guidance, refer to the following Partners policies:
Recruitment of Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects

https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf

Remuneration for Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf

CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own patients, describe how the potential for coercion will be avoided.

We will recruit and follow 69 pain patients for participation in this study. All patients will be currently treated at an outpatient clinic under Partners HealthCare.

Inclusion criteria for Patient Participants

- Must possess the ability to read and write English.
- Must be a patient with chronic low back pain.
- Must have a smartphone (either Android or iphone) and be able to download the pain app
- Must be willing to "agree" to participate in the study.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects:
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

Although the likelihood of any adverse events related to this study is considered remote, a data and safety monitoring plan will be in place. The plan is to ensure the safety of participants and the validity of data, as well as the termination of the study if a significantly adverse risk-benefit ratio is uncovered, or the study cannot be concluded successfully. The plan will be updated to make sure it complies with current local, state and federal policies, laws, and standards, for the conduct of research involving human participants. Unanticipated problems involving risks to subjects or others including adverse events will be reported to the PHRC in accordance with PHRC unanticipated problems reporting guidelines. Please refer to Partners Investigator's guidelines for unanticipated problems including adverse events reporting requirements.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

All data from the pain application will be stored in a secure Microsoft SQL Server database using SQL Server authentication. The database is housed on an isolated server within the Anesthesiology Department of Brigham and Women's Hospital with no remote access. All configuration files that store the database connection strings are encrypted on the web server and the program has passed Veracode testing. Study staff have the only access to this

database and the server itself is behind a firewall. Standard security practices will be used for administration accounts/services.

All data submitted via smartphone will immediately be transmitted and stored on a server located in a secure facility within the Anesthesiology Department. The server is located behind multiple firewalls. The Microsoft operating system on the servers is maintained and patched with all high priority and security related updates. Tunneling protocols and encryption are utilized to protect the transmission and storage of data whenever possible. Data transmitted contains answer codes and does not contain actual responses. The online database utilizes all the necessary security features to prohibit any unauthorized access. The database is specifically designed such that no identifying information is associated with the data collected. Server software performs security audits and real-time monitoring to immediately detect and warn of a security risk. Data back-ups are stored in a secure data vault. All electronic databases that contain data are located on a secure server and are password protected.

All data will be managed under the direction of the Principal Investigator. Research Coordinators will collect and ensure the completeness and accuracy of data. Questionnaire data will be entered into the computer manually. Data entry will be conducted using the application of standardized error-trapping and data-cleaning procedures including double entry of data. Original data are maintained in locked storage files and computer backup is conducted nightly. Identifying information, which may be necessary for follow-up procedures, will be kept separately under lock and key.

For guidance, refer to the following Partners policies:

Data and Safety Monitoring Plans and Quality Assurance
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP_in_Human_Subjects_Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting_Unanticipated_Problems_including_Adverse_Events.pdf

PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

To minimize the potential threat to loss of confidentiality (unauthorized access to participant data), the following procedures will be put in place:

State of the art security practices will be used when managing and storing the information collected from participants. Every reasonable effort will be made to ensure the confidentiality of participant information.

- Participant information will be kept in locked file cabinets or stored electronically on a secure computer server, accessible only to authorized research personnel.
- Any information collected from participants on a research form will be coded with a study-ID number and stored separately from participants' names or other identifying information. They cannot be linked to one another except by authorized research personnel with security authorization.
- Participant information will be used only for research purposes and will not be given out without their permission. Participants will not be identified in any publication or presentation, which may result from this research.
- All transfer of participant information through the smartphone pain app will be protected by a process called encryption, which changes the information so that only researchers at Brigham and Women's Hospital can read it.
- Participants' questionnaire responses will be coded with a study-ID number rather than participants' names or any other identifying information.
- Participants' identifying information and their smartphone app responses will be stored in separate electronic files. They cannot be linked to one another except by authorized research personnel with security authorization.
- All of the participants' information will be password-protected and kept on a firewall-protected computer server so no one but authorized personnel can access or view it.

There is always some risk to confidentiality when sending information over the Internet. Participants will be instructed to keep in mind that they may be observed, especially when using hospital-based computer systems. If any information about this study is reported or published, it will be in aggregate, meaning that only group data will be used, and individual name, information, or data will not be reported.

SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

Not applicable.

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

Not applicable.

RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the

specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

Not applicable.